



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
1401 Rockville Pike
Rockville MD 20852-1448

JAN 29 1997

Reference Numbers: 95-1773 and 95-1926

Mr. Julien Peetermans
SmithKline Beecham Biologicals
89, rue de l'Institut
1330 Rixensart
BELGIUM

Dear Mr. Peetermans:

Enclosed is a product license authorizing SmithKline Beecham Biologicals, U.S. License No. 1090, to import Diphtheria and Tetanus Toxoids and Acellular Pertussis Vaccine Adsorbed (DTaP), "Infanrix," for the primary and booster immunization of infants and children except as a fifth dose in children who have previously received four doses of DTaP, into the United States for sale, barter, or exchange.

Under this license you are authorized to manufacture Infanrix using Diphtheria and Tetanus Toxoids Adsorbed Combined Bulk manufactured by Chiron-Behring GmbH & Co. (U.S. License 1222) under a shared manufacturing arrangement. The product will be marketed in single dose vials.

The dating period for this product shall be 30 months from the date of manufacture when stored at 2-8°C, to include 12 months in manufacturer's storage and up to 24 months in distribution. The dating period of the final combination shall be based on the component with the shortest dating period and/or the first valid potency test, whichever period is the shortest [21 CFR 610.50(a) and 610.53(b)].

You are requested to submit to the Center for Biologics Evaluation and Research (CBER) samples of each future lot of product in final containers together with protocols showing the results of all applicable tests. No lots of product shall be distributed until notification of release is received from the Director, CBER.

We acknowledge the following commitments made in submissions dated October 28, 1996, and January 22, 1997:

1. You have agreed to submit, when available, the results of studies on the duration of protection of the vaccine in stage 3 of the NIH sponsored Italian Efficacy study.
2. You have agreed to submit a final report from study comparative immunogenicity and reactogenicity study of lots of Infanrix in which the pertussis

antigens were prepared using

fermenters, by June 1, 1997.

3. You will submit a finalized version of the mouse immunogenicity test for pertussis antigens by May 1, 1997.
4. You have agreed to submit the 30 and 36 month results of ongoing stability studies, including the results of mouse histamine sensitization studies at these same timepoints. In addition, you have agreed to include histamine sensitization as part of your stability assessment program.

This information will be placed on file in your Product License Application for this product.

Changes in the manufacture, testing, packaging or labeling of Diphtheria and Tetanus Toxoids and Acellular Pertussis Vaccine Adsorbed, in the supplier of the diphtheria and tetanus toxoids, or in the manufacturing facilities may require the submission of a Supplement to either your Product or Establishment License Application for our review and written approval prior to implementation.

If you wish to request extension of the dating period for this product you may do so by submitting a Supplement to your Product License Application along with documentation supporting the real-time stability of the product.

It is requested that adverse experience reports for Diphtheria and Tetanus Toxoids and Acellular Pertussis Vaccine Adsorbed, be submitted in accordance with the adverse experience reporting requirements for licensed biological products (21 CFR 600.80) and that distribution reports be submitted as described (21 CFR 600.81). Since your product is categorized as a vaccine, these reports should be submitted to the Vaccine Adverse Event Reporting System (VAERS) using the pre-addressed form VAERS-1.

Please submit three copies of final printed labeling at the time of use and include part II of the label transmittal form with completed implementation information. In addition, please submit three copies of the introductory advertising and promotional labeling. You may wish to submit the proposed materials in draft form with an FDA form 2567 to the Center for Biologics Evaluation and Research, Advertising and Promotional Labeling Staff, HFM-202, 1401 Rockville Pike, Rockville, MD 20852-1448. Promotional claims should be consistent with and not contrary to approved labeling. No comparative claims or claim of superiority over other similar products should be made unless data to support such claims are submitted to and approved by the Center for Biologics Evaluation and Research.

Please acknowledge receipt of the enclosed product license to the Director, Division of Vaccines and Related Products Applications, HFM-475, Center for Biologics Evaluation and Research.

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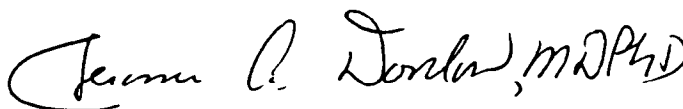
Also, your request to supplement your Establishment License Application to include areas for the manufacture of Diphtheria and Tetanus Toxoids and Acellular Pertussis Vaccine Adsorbed, in a shared manufacturing arrangement with Chiron-Behring GmbH & Co., Germany, has been approved.

The information contained in the above referenced supplement will be included in your establishment application file.

Sincerely yours,



M. Carolyn Hardegree, M.D.
Director
Office of Vaccines
Research and Review
Center for Biologics
Evaluation and Research



Jerome A. Donlon, M.D., Ph.D.
Director
Office of Establishment Licensing
and Product Surveillance
Center for Biologics
Evaluation and Research

cc: Clare Kahn, Ph.D.